CS14-04 The Development of an AIDS Mucosal Vaccine

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Mucosal vaccination offers great advantage for inducing protective immune response at the sites of viral transmission. A novel replication-competent modified vaccinia Tian Tan (MVTT) is an attenuated variant of the wild-type VTT, which was historically used as a smallpox vaccine for millions of people in China. MVTT was generated through genetic engineering and clonal selection of VTT and exhibited excellent safety profiles for mucosal inoculation. The spike glycoprotein (S) of SARS-CoV was used as a test antigen after the S gene was constructed in the identical genomic location of two live vectors to generate vaccine candidates MVTT-S and MVA-S. A head-to-head comparison has been conducted in mice for inducing neutralizing antibodies (Nabs) via mucosal vaccination. Our results indicated that MVTT is superior to MVA for inducing high levels of systemic Nab response post mucosal vaccination. Moreover, a candidate vaccine MVTT-SIVgpe, which expresses three major viral structural proteins of simian immunodeficiency virus, has been recently characterized in vitro. The efficacy of MVTT-SIVgpe will be further evaluated in a highly pathogenic SIV/Chinese macaque model.

Concurrent Session 15 – Hepatitis and HCC

CS15-01 Can We Prevent Hepatocellular Carcinoma in Chronic Hepatitis B?

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Hepatitis B virus (HBV) infection is the commonest cause of hepatocellular carcinoma (HCC) most countries in Asia. After the launching of the universal vaccination program, the incidence of childhood HCC has been dramatically reduced in Taiwan. As HCC in adult commonly develop at the age the 40 to 50 years, it may take another 20 to 30 years before one can see a significant reduction in incidence of adult HCC.

Clearance of HBsAg is the marker of ultimate viral control in chronic hepatitis B. If HBsAg clearance occurs before the age of 50, the prognosis is excellent. However, spontaneous HBsAg clearance is rare. Peginterferon and oral antiviral agents can induce HBsAg clearance in about 10% and 5% of patients, respectively. High HBV DNA has been found to associate with higher risk of HCC. However the data from individual studies on the long term benefit of interferon or antiviral agent is conflicting.

A meta-analysis has been conducted to investigate the beneficial effect of interferon and antiviral agents (mainly lamivudine) on HCC. Interferon is associated with an approximate 33% reduction in risk of HCC. Lamivudine is associated with an approximate 80% reduction in risk of HCC.

In summary, vaccination can prevent HCC by preventing HBV infection. HBsAg clearance in an early age can almost prevent HCC. Interferon and antiviral treatment can reduce the risk but not completely prevent HCC.

CS15-02 Current Japanese Strategies for Preventing HCC Development

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In Japan, the death caused by liver disease is still major problems in health care. Most importantly, the death from liver diseases exceeds 30,000 cases in Japan. Approximately, nearly 80% of these death is derived from hepatitis C virus (HCV) related liver diseases, namely hepatocellular carcinoma (HCC).

Although the incident of HCV infections is decreasing in Japan due to current screening strategies, the patients with established infections have reached their most susceptible stage for developing HCC. In other words, the Japanese patients with HCV infection are facing highest risk for developing HCC. The current preventive strategies for developing HCC includes antiviral therapy, namely interferon based regimen. However, the results of current standard therapy, PEG-interferon plus ribavirin treatment, is not satisfactory in genotype 1b with high viral load, which is most commonly observed population in Japan and US. The recent reports have documented up to 50% of the patients treated with antiviral therapy eradicated HCV genotype 1b infection. Moreover, the adherence to the antiviral therapy is poorly tolerated in elderly populations, which is now biggest patients' population in Japan. Thus, in Japanese society, the eradication of HCV itself seems more and more difficult. Moreover, the social benefit regarding antiviral treatment in elderly patients, especially above 70 years old, has not been established. The patients in this age have the highest risk for developing HCC and poorest results after antiviral treatment. Furthermore, these patients tend to be intolerant to the interferon based treatment. Adverse effects such as depression are more commonly observed in these elderly patients. Besides these anti-viral treatments, so-called maintenance therapies are frequently applied to these elderly populations. Low-dose interferon monotherapy, oral intake of ursodeoxy cholic acids, and phlebotomy are included in these maintenance therapies. However, the recent results from HALT-C gave questions about the rational of long-term interferon monotherapy. Thus, the evidences for preventing HCCs by these maintenance therapies seem to be weak.

In summary, the Japanese strategies for preventing HCC development is; i) eradicate the possible as early as possible since the adherence to the standard antiviral treatment is poor in elderly patients with HCV, ii) perform social education for understanding the natural course of HCV infection to accept the early eradicative treatment, iii) establish the social supportive program to receive antiviral therapy (both medical and economical), and iv) develop interferon free based antiviral treatment to increase the adherence of antiviral therapy in elderly populations.

CS15-03 Prevention of HCC Related to Viral Hepatitis

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CS15-04 The Role of Polo-like Kinase 1 as a Therapeutic Target in Hepatocellular Carcinoma

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Polo-like kinase 1 (PLK1) plays important roles in the progression of cell cycle, especially for cells transiting from anaphase to telophase during mitosis. PLK1 has been found to be overexpressed in various cancers, and has important prognostic implications.

Methods: PLK1 gene expression was evaluated in Hepatocellular carcinoma (HCC) and found to be overexpressed frequently in HCC tissues. Gene silencing technology utilizing short interfering RNA (siRNA) was subsequently employed to study the potential of PLK1 to be the therapeutic target in treating HCC. Knockdown with si-RNA was performed to examine for reduction in cell proliferation using MTS and BrdU assays, after validating reduced expression by real-time PCR (RTPCR) and Western Blotting. Confirmation of apoptosis was performed using TUNEL assay, and subsequent pathway of apoptosis was examined using a caspase-inhibition assay. Experiments with transplanted tumour cell lines into nude mice co-cultured with si-RNA against the target gene, and examining for reduced tumour progression compared to controls was performed.

Results: Microarray analysis showed the most common over-